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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/717,101	11/19/2003	Harold L. Atkins	18013-C1	7313

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/717,101	ATKINS ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *10-16 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 17, 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/03/&02/06/2004*. 03/15/2005
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The preliminary amendment filed November 19, 203 has been acknowledged. The specification regarding to the priority has been amended.

Election/Restrictions

1. Applicant's election of Group I, claims 8-9 in the reply filed on 01/03/2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-9 and 17-24 are encompassed in the elected group since claims 1-7 and 17-24 are linking claims.

2. Upon considering all elected claims, the examiner notices that the claims directed to the following patentably distinct species of the claimed invention: A). The virus is a replication competent RNA virus, and B). The virus is a replication-incompetent RNA virus because the replication-incompetent virus is structurally and functionally different from the replication-competent virus. Each of them has different patentable weight and requires a different search.

3. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 2 is generic.

4. During a telephone conversation with Applicants' representative Lewis Kreisler on March 18, 2005, a provisional election was made species A) of replication-competent RNA virus without traverse to prosecute the invention of species A) of claim17. Affirmation of this election must be made by applicant in replying to this Office action. Claim18 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which ones are readable upon the elected species. MPEP § 809.02(a).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the

currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

7. Therefore, claims 1-9, 17, and 19-24 are considered.

Specification

The disclosure is objected to because of the following informalities: In line 1 of page 3, there is an improper handwriting inserted. If this is an amendment, it has to be done officially in a proper way. An appropriate correction is required.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence(s) of the specification or in an application data sheet by identifying the prior application by application number (37 CFR 1.78(a)(2) and (a)(5)). If the prior application is a non-provisional application, the specific reference must also include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 20 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 20 and 21 are failed to point out to where the claimed chemotherapeutic agent or an interferon are administered before and after contacting with claimed oncolytic virus ex vivo. It is unclear whether the claimed chemotherapeutic agent or interferon is added into the mixture

comprising neoplastic cells and normal cells or into population of normal cells or population of neoplastic cells respectively or into a patient who is undergoing the claimed autologous or allogenic transplantation before the mixed populations of normal hematopoeitic cells and neoplastic cells are isolated or placed back after the treatment by the claimed oncolytic virus.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-8, 17, 19-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for utilizing a replicating-competent vesicular stomatitis virus (VSV) to selectively kill acute myelogenous leukemia cell mixed with normal hematopoeirtic cells in an in vitro setting system, does not reasonably provide enablement for an ex vivo method of utilizing any or all virus to purge all kinds of neoplastic cells, wherein the method further comprises treating the mixture with a chemotherapeutic agent or interferon before, during and after contacting with the virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in the scope with these claims.

13. The test of scope of the enablement is considered whether one skilled in the art could make and use the full scope of the claimed invention from the disclosures in the application coupled with information known in the art without doing undue experimentation in view of the Wands factors (MPEP 2164.01(A). These factors include: (1) nature of the invention, (2) scope of the claims, (3) guidance of the specification, (4) the existence of working example, (5) state of art, (6) predictability of the art and (7) the amount of the experimentation necessary.

14. 1) Nature of the invention. The invention is drawn to a method of selectively killing the contaminated acute myelogenous leukemia cells in the mixture of normal bone marrow cells isolated from a health person with a replication-competent VSV in vitro.

15. 2). Scope of claims. The scope of claims is broadly drawn to an ex vivo method of purging any or all kinds of neoplastic cells contaminated in normal hematopoeitic cells with any kind of virus, wherein the ex vivo method further comprises treating the engrafting mixture with a chemotherapeutic agent or interferon before, during and after contacting the oncolytic virus.

16. 3) &4) State of art and unpredictability. Oncolytic ("onco" meaning cancer, "lytic" meaning "killing") viruses represent an special group of viruses that capable of selectively destructing tumor cells directly by the viral replication or indirectly via expressing a therapeutic toxic gene product to kill the cancer cells as taught by Kirn et al. (The Molecular Medicine Today, 1996, pp. 519-527). An oncolytic virus can be naturally isolated virus or genetic engineered virus (2002 Cell Genesys. Inc. website: http://www.cellgenesys.com). Apparently, not every virus is an oncolytic virus. For example, lots of native viruses are not oncolytic viruses because they kill the neoplastic cells as well as normal cells. For example, HIV is a virus that is capable of killing neoplastic cells H9 lymphoma cells (cell line repository in NIH AIDS reagent repository catalog, page 3) as well as cells normal T cells that express HIV CD4 receptor and CXCR4 co-receptor as taught by Robert C. Mellors (Pathogenesis of HIV infection and AIDS published on 1999 at website of Cornell University Medical College: http://edcenter.med.conell.edu/CMMC_pathNotes/HIV_infection/HIV_infection_04.html). Therefore, it is unpredictable of using all viruses as an ex vivo treatment of a cancer.

17. VSV is a single strand, non-segmented, negative sense RNA virus that belongs to rhabdovirus family. The native isolated replication –competent VSV exhibits its oncolytic activity via direct viral replication against particular groups of tumors that bear abnormal p53, ras or myc gene. Although VSV infection is extremely sensitive to the antiviral actions of interferons (INFs), the researchers found that the replicating-competent VSV is able to inhibit wide variety of malignant tumors that harbor aberrant tumor suppresser gene p53, proto-oncogene ras and myc in spite of the tumor cells contain a functional INF/PKR system as evidenced by Balachandran et al. (J. Virol. 2001, Vol. 75, No. 7, pp. 3474-3479, see 1st paragraph of page 3474). However, not all native replication-competent rhabdovirus can be used for the claimed ex vivo oncolytic treatment. For example, Rabies virus is a non-segmented, negative sense, RNA rhabdovirus that can lyses target cells as evidenced by Coulon et al. (J. Virol. 1989, Vol. 63, No. 8, pp. 3550-3554, see abstract), but it is not safe for using it as an

oncolytic virus to treat a neoplasm. Because a native high neurovirulent rabies virus infection is so fatal that no infected patients have survived as reported by CDC (Rabies nature history published by CDC December, 2003, see Table 6 on page372).

18. State of art also teaches that different oncolytic virus has different susceptibility to replicate well in certain type of tissues as evidenced by Kirn et al. (The Molecular Medicine Today, 1996, pp. 519-527, see Table 1 on page 522) or certain type of oncogene expressed neoplasm as taught by Strong et al. (The EMBO J. 1998, Vol. 17, No. 12, pp. 335-3362) and Balachandran et al. as described above. For example, reovirus can preferentially replicate well in oncolytic in proto-oncogene ras-transformed neoplasm and selectively kill the neoplastic cells over the non-ras mutated normal cells since the activation of the mutated Ras oncogene prohibits the host cell interferon/protein kinase R signal pathway as evidenced by Strong et al. see abstract). A cancer can be induced by many proto-oncogene or tumor suppressor gene mutations rather then p53, *ras* and myc. For example, breast cancer can be induced p27, BRCA-1, BRCA-2, CHK2, ATM, PTEN and Rb as evidenced by Osborne et al. (The oncologist 2004, Vol. 9, pp. 361-377). Therefore, it is unpredictable that every virus can replicate well in every type of neoplastic cells and selectively kill the neoplastic cells over the normal hematopoeitic cells, especially in an interferon resistant way as claim 21 drafted.

19. 5) & 6). Working examples and amount of guidance presented in the specification. The specification of current application only teaches that replication-competent VSV is able to selectively kill the acute myelogenous leukemia cells lines, OCI/AML3, OCI/AML4 or OCI/AML5 in a mixture comprising a normal bone marrow cells isolated from the health persons in an in vitro setting system. Applicants also teach that VSV is resistant to interferon treatment in ovarian carcinoma, lung cancer, melanoma, prostate carcinoma, colon carcinoma and an immortalized human kidney cell lines 293T. However, the specification does not provide sufficient evidences supporting that any or all viruses can selectively kill any neoplastic cells over an autologous or allogenic isolated normal hematopoeitic cells in the presence of an interferon treatment.

20. For example, the specification does not teach that any neoplasm can be selectively killed with all oncolytic viruses over other non-tumor cells ex vivo. The specification even does not provide sufficient evidenced to support that other neoplasm rather than myelogeous leukemia

will be selectively killed by VSV in the mixture ex vivo sample, such as a breast cancer induced by Rb or BRCA-2 gene expression. The specification lacks of teaching and sufficient guidance about how to select a specific virus that susceptibly replicate well in a certain type of neoplasm and preferably kills the neoplasm over other normal peripheral hematopoeitic cells. The specification does not teach that the claimed VSV is able to replicate well in acute myetogeneous leukemia cell lines OCI/AML3, OCI/AML4 or OCI/AML5 in the presence of an interferon. The specification is deficient for teaching whether administration of interferon during other oncolytic virus treatment will affect the virus replication or if any of such virus exist, which kind of neoplasm will support the virus replication. Because it is well known in the art that all of virus without specific gene mutation will response to the interferon treatment. Therefore, it is unpredictable to administer any or all virus in the presence of interferon.

21. 7). Amount of the experimentation necessary. Based on the broad scope of claims, the person skilled in the art has to test each of available viruses for its oncolytic activity on each kind of neoplasms.

22. Therefore, considering the unpredictability of the field, it must be considered that the skilled artisan would have to conduct undue experimentation in order to practice the full scope of claimed invention.

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887,225 USPQ 645 (fed. Cir. 1985).

25. In the instant case, claims 1-2 and 6-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 35 of copending Application No. 09/664,444 in view of Weber et al. (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and Rummel et al. (J. Hematotherapy 1994, Vo. 3, pp. 213-218) because:

26. Claims 1-2 and 6-9 of current application are drawn to an ex vivo method for purging neoplastic cells in the presence of normal hematopoeitic cells by contacting said mixture with VSV. Claim 35 of application 09/664,444 is drawn to a method for reducing the viability of a tumor cell in a population comprising tumor cells and non-tumor cells by administering VSV to the mixed cell population. Therefore, both sets of claims are directed to a method of reduction of neoplastic cell numbers in population of cells comprising non-tumor cells and tumor cells by VSV in vitro.

27. While the reference claim 18 is drawn to all non-tumor cells in general, and rejected claims in current application is drawn to normal hematopoeitic cells in particular, it is well known in the art that purging tumor cells ex vivo can only be done with hematopoeitic stem cells in cancer autologous transplantation therapy because the major source for the non-tumor cells that are able to differentiate to other lineage of cells are hematopoeitic stem cells. No other cell in the body has such differentiation ability. Secondly, most cancer is metastasized through the blood circulatory system to bone, which is the bank of hematopoeitic stem cells as evidenced by Weber et al. (See abstract). Consequently, the great concern in the autologous hematopoeitic

stem cell transplantation is the contamination of the grafting cells with metastatic cancer cells as evidenced by Rummel et al. (J. Hematotherapy 1994, Vol. 3, pp. 213-218, see abstract). Therefore, a person with ordinary skill in the art in order to get the best result of purging the contaminated engrafting cells ex vivo would have been obviously to purge the hematopoeitic cells with VSV. Hence, the claimed invention is a best and an obvious choice over the generically claimed normal non-tumor cells in the conference claim.

28. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

29. Claims 1-2, and 6-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 18 of copending Application No. 10, 743, 639 in view of Weber et al. (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and Rummel et al. (J. Hematotherapy 1994, Vo. 3, pp. 213-218) because:

30. Claims 1-2 and 6-9 of current application are drawn to an ex vivo method for reducing or eliminating neoplastic cells in mixture of normal hematopoeitic cells and neoplastic cells by contacting said mixture with the non-segmented, single stranded, negative sense RNA virus, VSV. Claim 18 of application 10,743,639 is drawn to a method for reducing the viability of a tumor cell within a population of tumor cells and non-tumor cells comprising administering a VSV to the population of cells, wherein the tumor cells are melanoma cells. Hence, both sets of claims are directed to a method of reduction of neoplastic cell numbers mixed with non-tumor cell population by VSV in vitro after the mixed populations of cells are withdrawn from an animal body. While the tumor cell that claim 18 is directed to a specific carcinoma, it is a species of the neoplasm cell, and it is encompassed within the broad scope of genus of a neoplasm.

31. While the reference claim 18 is drawn to all non-tumor cells in general, and rejected claims in current application is drawn to normal hematopoeitic cells in particular, it is well known in the art that purging tumor cells ex vivo can only be done with hematopoeitic stem cells in cancer autologous transplantation therapy because the major source for the non-tumor cells that are able to differentiate to other lineage of cells are hematopoeitic stem cells. No other cell in the body has such differentiation ability. Secondly, most cancer is metastasized through the blood circulatory system to bone, which is the bank of hematopoeitic stem cells as evidenced by

Weber et al. (See abstract). Consequently, the great concern in the autologous hematopoeitic stem cell transplantation is the contamination of the grafting cells with metastatic cancer cells as evidenced by Rummel et al. (J. Hematotherapy 1994, Vol. 3, pp. 213-218, see abstract). Therefore, a person with ordinary skill in the art in order to get the best result of purging the contaminated engrafting cells ex vivo would have been obviously to purge the hematopoeitic cells with VSV. Hence, the claimed invention is a best and an obvious choice over the generically claimed normal non-tumor cells in the conference claim.

32. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

33. Claims 1-2, and 6-9 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable distinct over claim 18 of copending Application No. 10,743,649 in view of Weber et al. (Crit. Rev. Eukaryot Gene Expr. 2000, Vol. 10, No. 3-4, pp. 281-302) and Rummel et al. (J. Hematotherapy 1994, Vo. 3, pp. 213-218) because:

34. Claims 1-2, and 6-9 of current application are drawn to an ex vivo method for reducing or eliminating neoplastic cells in mixture of normal hematopoeitic cells and neoplastic cells by contacting said mixture with the non-segmented, single stranded, negative sense RNA virus, VSV. Claim 18 of application 10,743,649 is drawn to a method for reducing the viability of a tumor cell within a population of tumor cells and non-tumor cells comprising administering a VSV to the population of cells, wherein the tumor cells are melanoma cells. Hence, both sets of claims are directed to a method of reduction of neoplastic cell numbers mixed with non-tumor cell population by VSV in vitro after the mixed populations of cells are withdrawn from an animal body. While the tumor cell that claim 18 is directed to a specific melanoma, it is a species of the neoplasm cell, and it is encompassed within the broad scope of genus of a neoplasm.

35. While the reference claim 18 is drawn to all non-tumor cells in general, and rejected claims in current application is drawn to normal hematopoeitic cells in particular, it is well known in the art that purging tumor cells ex vivo can only be done with hematopoeitic stem cells in cancer autologous transplantation therapy because the major source for the non-tumor cells that are able to differentiate to other lineage of cells are hematopoeitic stem cells. No other cell in the body has such differentiation ability. Secondly, most cancer is metastasized through the

blood circulatory system to bone, which is the bank of hematopoeitic stem cells as evidenced by Weber et al. (See abstract). Consequently, the great concern in the autologous hematopoeitic stem cell transplantation is the contamination of the grafting cells with metastatic cancer cells as evidenced by Rummel et al. (J. Hematotherapy 1994, Vol. 3, pp. 213-218, see abstract). Therefore, a person with ordinary skill in the art in order to get the best result of purging the contaminated engrafting cells ex vivo would have been obviously to purge the hematopoeitic cells with VSV. Hence, the claimed invention is a best and an obvious choice over the generically claimed normal non-tumor cells in the conference claim.

36. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

37. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

38. Claims 1, 2, 4, 5, 17 and 24 are rejected under 35 U.S.C. 102 (anticipated) as being anticipated by Belch et al. (Blood, 1998, Vol. 92, No. 10, Suppl. 1, part 1-2, 4th Annual Meeting of the American Society of Hematology; Miami Beach, Florida, USA; 2-8, December 1998, Abstract 426).

39. Belch et al. teach a method of ex vivo purging the multiple myeloma (MM) cell from the bone marrow and blood isolated from the same patient who suffered from the MM. The method comprises to drawn the MM contaminated blood cells and bone marrow cells from the patients and co-culture the cells mixture with reovirus, wherein the reovirus is a replication-competent RNA virus (See the last paragraph). Therefore, the claims 1, 2, 4, 5, 17 and 24 are anticipated by the cited reference.

40. Claims 1, 4, 5 and 17 are rejected under 35 U.S.C. 102 (b) as being anticipated by Seth et al. (Cancer Research 1996, Vol. 56, No. 6, pp. 1346-1351).

41. Seth et al. teach a method of ex vivo purging breast cancer cells contaminated normal bone marrow (BM) and G-MCSF-mobilized normal peripheral blood cells with adenovirus carrying p53 gene, wherein the breast cancer cells are selectively killed by the adenoviral vector ex vivo (See pages Fig. 5 and paragraphs on page 1349). Therefore, the claims 1, 4, 5 and 17 are anticipated by the cited reference.

42. Claims 1, 4, 5 and 17 are rejected under 35 U.S.C. 102 (b) as being anticipated by Marini et al. (Clinical Cancer Research 1999, Vol. 5, pp. 1557-1568).

43. Marini et al. teach a method of ex vivo purging the human breast cancer cells (BCC) in the mixture of autologous bone marrow (BM) or peripheral blood cell (PB-SC) with adenovirus carrying GAL-TEK gene marker/suicide gene followed by ganciclovir (GCV) treatment (See abstract). The BCC and bone marrow cells as well as PB-SC are all drawn for the same patient and the mixed populations of cells are infected with the adenoviral vector ex vivo. The BCC is selectively reduced due to the cytotoxicity effect carried by the therapeutic cytotoxic gene in the adenoviral vector (See pages 1558-1559, especially Fig. 4 on 1564). Therefore, the claims 1, 4, 5 and 17 are anticipated by the cited reference.

Claim Rejections - 35 USC § 102

44. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

45. Claims 1-5, 17 and 19, 20, 22-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Morris et al. (A) (US Pub. No. 2001/0048919A1).

46. Morris et al. (A) teach an ex vivo method of eliminating ras-activated neoplasm cells comprising contacting a population of autologous cells suspected of having such neoplastic cells with reovirus, wherein the method comprises harvesting the autologous hematopoeitic stem cells from bone marrow or blood of a cancer patient, contacting the mixture of autologous cells with reovirus and then transplanting the treated cellular mixture back to the patient (See abstract and paragraph 0077, claims 1-4, 9-10), hereby the reovirus selectively kill the ras-mediated neoplasm. Morris et al. teach that neoplasm include benign or malignant tumor, such as leukemia and lymphoma (Paragraph 0083). Morris et al. also disclose that another embodiment of their inventing is to stimulate the host immune system (See paragraph 0147), and the cancer patient who is involved in the ex vivo autographic transplantation received a traditional high does of chemotherapy before the ex vivo virus treatment (See paragraph 0114). Therefore, the claimed invention is anticipated by the cited reference.

47. It should be noted that the above rejections are based the disclosures of Morris et al.(A) that are supported by its priority document of provisional application SN. 60/205,389, filed on May 19, 2000 (See claims 1-17, lines 26-29 on page 9 and lines 2-12 on page 10).

48. Claims 1-5, 17, 19 and 20, 22-24 are rejected under 35 U.S.C. 102(e) as being anticipated by Morris et al. (B) (US Pub. No. 2001/0048919A1).

49. Morris et al. (B) teach an ex vivo method of eliminating ras-activated neoplasm cells comprising contacting the RNA reovirus with a population of autologous cells suspected of having such neoplastic cells, wherein the method comprises harvesting the autologous hematopoeitic stem cells from bone marrow or blood of a cancer patient, contacting the mixture of autologous cells with reovirus and then transplanting the treated cellular mixture back to the patient, hereby the reovirus selectively kill the ras-mediated neoplasm. The method also comprises a step of administering at least one substance selected from the group consisting of anti-reovirus antibody and an immune system stimulating agent (See paragraph 0039). Morris et al. teach that neoplasm include benign or malignant tumor, such as leukemia and lymphoma (Paragraph 0058). Morris et al. also disclose that the cancer patient who is involved in the ex vivo autographic transplantation received a traditional high does of chemotherapy before the ex vivo virus treatment (See paragraph 0080, 0081 and 0027).

50. It should be noted that the above rejections are based the disclosures of Morris et al.(A) that are supported by its priority document of provisional application SN. 60/205,389, filed on May 19, 2000 (See claims 1-17, lines 26-29 on page 9 and lines 2-12 on page 10).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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03/18/2005